UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,498	06/01/2001	Adilson Leite	FAPESP 203	8814

24972 7590 09/11/2006

FULBRIGHT & JAWORSKI, LLP
666 FIFTH AVE
NEW YORK, NY 10103-3198

EXAMINER	
SRIVASTAVA, KAILASH C	
ART UNIT	**PAPER NUMBER**
1655	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,498	LEITE ET AL.	
	Examiner	Art Unit	
	Dr. Kailash C. Srivastava	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 8-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1 Applicants' responsive communication filed 25 May 2006 in response to Office Action mailed 04 May 2006 is acknowledged and entered.

2. Once a response/filing arrives at the United States Patent and Trademark Office (i.e., USPTO), the claims, remarks, amendments etc., are separated for proper coding to scan them in the electronic file wrapper (i.e., IFW). In order to ensure that all the papers pertaining to a particular application are properly coded in the same application electronic file wrapper, and to further facilitate the prosecution; especially during a telephonic conversation/interview with applicants/applicants' representative, it is suggested that in the header of the each page for any filing/response/amendment, the following information be recited:

a. U.S. Non-Provisional application Serial Number;
b. Filing date for said application (e.g., 01 June 2001);
c. First Applicant's name (e.g., Smith Jones);
d. Attorney Docket Number;
e. Group Art Unit Number (e.g., 1655);
f. Examiner's name (e.g., Dr. Kailash C. Srivastava);
g. Date of Office Action being responded to; and
h. Date of amendment/response.

Papers/responses filed according to above-stated guidelines immensely ameliorate the chances of papers lost during transaction/transmission, coding, indexing and placing the papers in IFW.

CLAIMS STATUS

3. Claims 1-29 are pending.

Restriction/Election

4. Applicants' election of Group I, Claims 1-8 filed 20 December 2005 in response to Office Action mailed 29 November 2005 is acknowledged and entered. Since the election is made without traverse, the restriction requirement is deemed proper and is made FINAL

Accordingly Claims 1-4 and 8-28 have been withdrawn from further action. See 37 CFR §1.142(b) and MPEP § 821.03. Examiner recommends that in response to this Office Action, the non-elected claims cited *supra* be canceled to expedite prosecution.

5. Claims 5-7 and 29 are examined on merits.

Claims Objection

6. Claim 29 is objected to for following reasons:

- Claim 29 is objected to because at Line one of the cited Claim, before the word "wherein" a --, -- should be inserted. Appropriate correction is required.

Objection To Oath

7. Under MPEP §060506, the person making the oath or declaration believes the named inventor or inventors to be the original and first inventor or inventors of the subject matter which is claimed and for which a patent is sought. During search for prior art, however, a foreign application is found wherein the specification, abstract, claims and drawings are identical to instantly presented application, but named inventors are only Adilson Leite and Urara Kawazoe, rather than the instantly named four inventors (i.e., Adilson Leite, Urara Kawazoe, Paulo Arruda and Arnaldo da Silva Junior). Consequently, Examiner is not clear about the inventorship of the claimed invention. Burden of clarification/correction of inventorship is on the applicants. Appropriate correction/clarification is required.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> ***(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention of***

9. Claims 5-7 and 29 are rejected under 35 U.S.C. § 103 (a) as obvious over the combined teachings from Ford et al. (US Patent 6,497,870 B1) in view of Aley et al (Infection and Immunity, 1994, Volume 62, pages 5397-5403) and Janoff et al. (U S Patent 5,766,624) with evidence provided by De Samblanx et al (U.S. Patent 6,372, 888 B1).

Claims recite an isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues, wherein said peptide is comprised of 10-12 contiguous amino acids of which 7 are hydrophobic, 3 are basic and at least one is one among histidine, glutamic acid or serine with two of the hydrophobic residues comprised of adjacent tryptophan residues. Additionally said peptide comprises amino acid sequence in SEQ ID NO: 1 or a conservative variant for said SEQ ID NO.

Ford et al teach a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an active variant thereof that differs from the natural polypeptides by amino acid insertion, deletion and substitutions, said variants having up to 95% or higher sequence identity to SEQ ID NO: 1 and retained the biological activity. (Column 8, Lines 8-20). Ford et al. further teach replacement of said amino acid residues having similar structure/function relationships and are therefore conservative replacements. Among the conservative properties for amino acid residues to be substituted, Ford et al teach hydrophobicity, hydrophilicity, amphipathy of substituted residues and further teach at least 7 hydrophobic residues, additionally serine and histidine and also tryptophan (Column 8, Lines 3045; Column. Thus, Ford et al teach a polypeptide comprised of same amino acid residues and having same structure functional relationship, that of having antimalignancy properties as is instantly claimed.

Ford et al., however, do not explicitly teach said isolated peptide to be antimicrobial and amidated, carboxymethylated or cyclized and exhibiting low toxicity to animal and plant cells.

Aley et al. teach isolated antimicrobial polypeptide, i.e., defensins and indolicidins that have nine highly conserved amino acid residues (Page 5397, Column 1, Lines 38-43; are uniquely tryptophan rich (Abstract Lines 15-16) and additionally has C-terminal amide (Page 5397, Column 2, Lines 31-34). Aley et al. further teach that said polypeptides have conservative substitutions, have amphipathic surface topology (Page 5400, Column 2, below Figure 4, Lines 5-15). Janoff et al teach that defensns and indolicidins are microbicidal, tumorocidal cytotoxic and less toxic at concentration of up to 230 g/mL to animal cells (Abstract, Lines 1-3; Figure 8-10 and 13; Column 24- Lines 24-34). Note that defensins are also known from plants and are not toxic to plant cells as well because they are produced in plants to combat pest-attack (see De Samblanx et al. abstract, Column 1, Lines 35-38).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify Ford et al's teachings with those from Aley et al's and Janoff et al with Support from De Samblanx et al., to obtain the claimed antimicrobial, polypeptide having the amino acid sequence of SEQ ID NO: 1 or an active variant thereof, because Ford et al. teach an anti-malignancy polypeptide having the amino acid sequence of SEQ ID NO: 1 comprised of same amino acid residues and having same structure function relationships as well as substitutions, Aley et al. teach that defensins ands and indolicidins are isolated antimicrobial peptides are rich in tryptophan, have at least 9 highly conservative amino acid residues and amidated c-terminus and Janoff et al. teach that defensins and indolicidinss are antimicrobial, tumericidal polypeptides having less toxicity to animal and plant cells.

One having ordinary skill in the art at the time of the claimed invention would have been motivated to modify/combine the teachings from Ford et al's teachings with those from Aley et al's and Janoff et al with Support from De Samblanx et al., to obtain the claimed antimicrobial, polypeptide having the amino acid sequence of SEQ ID NO: 1 or an active variant thereof as discussed in the previous paragraph.

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

PRIOR ART

10. The following prior art made of record and not relied upon is considered pertinent to Applicants' disclosure.

- Selsted, M.E. et al., On Dolicifdin, a novel Bactericidal tridecapeptide Amide from Neutrophils. 1992. The Journal of Biological Chemistry, Volume 272, Pages 4292-4295

Claim Rejections - 35 U.S.C. § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 5-7 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The claimed are drawn to an isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues, wherein said peptide is comprised of 10-12 contiguous amino acids of which 7 are hydrophobic, 3 are basic and at least one is one among histidine, glutamic acid or serine with two the hydrophobic residues comprised of adjacent tryptophan residues. Additionally said peptide comprises amino acid sequence in SEQ ID NO: 1 or a conservative variant for said SEQ ID NO:1.

From the record of the presently filed written disclosure, the specification enables for every other description for a peptide with identical amino acid sequence for Sequence ID. NO: 1 except an isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues, wherein said peptide is comprised of 10-12 contiguous amino acids of which 7 are hydrophobic, 3 are basic and at least one is one among histidine, glutamic acid or serine with two of the hydrophobic residues comprised of adjacent tryptophan residues. Additionally said peptide comprises amino acid sequence in SEQ ID NO: 1 or a conservative variant for said SEQ ID NO. The specification as presented (see Examples 1-4) does not reasonably provide support to demonstrate an "isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cell and having the amino acid sequence of Sequence ID No: 1". Thus, in the absence of demonstrated evidence of record that said isolated peptide was actually isolated, the claimed invention is not considered to have been in inventors' possession at the time of said invention.

13. Claims 5-7 and 20 are rejected under 35 U.S.C. 112, first paragraph as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to an isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues, wherein said peptide is comprised of 10-12 contiguous amino acids of which 7 are

hydrophobic, 3 are basic and at least one is one among histidine, glutamic acid or serine with two of the hydrophobic residues comprised of adjacent tryptophan residues. Additionally said peptide comprises amino acid sequence in SEQ ID NO: 1 or a conservative variant for said SEQ ID NO: 1.

From the record of the presently filed written disclosure, the specification enables for every other description for a peptide with identical amino acid sequence for Sequence ID. NO: 1 except an isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues, wherein said peptide is comprised of 10-12 contiguous amino acids of which 7 are hydrophobic, 3 are basic and at least one is one among histidine, glutamic acid or serine with two of the hydrophobic residues comprised of adjacent tryptophan residues. Additionally said peptide comprises amino acid sequence in SEQ ID NO: 1 or a conservative variant for said SEQ ID NO. The specification as presented (see Examples 1-4) does not reasonably provide support to demonstrate an "isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cell and having the amino acid sequence of Sequence ID No: 1". Thus, in the absence of demonstrated evidence of record that said isolated peptide was actually isolated, the claimed invention is not considered enabled.

A person of skill would not be able to practice the invention because undue experimentation will be required to obtain claimed invention. The person of skill will not be able to practice the claimed invention due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Undue experimentation will be necessary because there is no recited guidance, i.e., how to obtain the instantly claimed isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues as recited in the claimed invention.

14. Claims 5-7 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the claimed composition does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims are drawn to an isolated antimicrobial amidated, carboxymethylated or

cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues, wherein said peptide is comprised of 10-12 contiguous amino acids of which 7 are hydrophobic, 3 are basic and at least one is one among histidine, glutamic acid or serine with two of the hydrophobic residues comprised of adjacent tryptophan residues. Additionally said peptide comprises amino acid sequence in SEQ ID NO: 1 or a conservative variant for said SEQ ID NO: 1.

From the record of the presently filed written disclosure, the specification enables for every other description for a peptide with identical amino acid sequence for Sequence ID. NO: 1 except an isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues, wherein said peptide is comprised of 10-12 contiguous amino acids of which 7 are hydrophobic, 3 are basic and at least one is one among histidine, glutamic acid or serine with two of the hydrophobic residues comprised of adjacent tryptophan residues. Additionally said peptide comprises amino acid sequence in SEQ ID NO: 1 or a conservative variant for said SEQ ID NO. The specification as presented (see Examples 1-4) does not reasonably provide support to demonstrate an "isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cell and having the amino acid sequence of Sequence ID No: 1". Thus, in the absence of demonstrated evidence of record that said isolated peptide was actually isolated, the claimed invention is not considered enabled.

A person of skill would not be able to practice the invention because undue experimentation will be required to obtain claimed invention. The person of skill will not be able to practice the claimed invention due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Undue experimentation will be necessary because there is no recited guidance, i.e., how to obtain the instantly claimed isolated antimicrobial amidated, carboxymethylated or cyclized peptide exhibiting low toxicity to animal and plant cells, having up to 50 amino acid residues as recited in the claimed invention.

Conclusion

15. For reasons aforementioned, no Claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Terry McKelvey, can be reached on (571)-272-0775 Monday through Friday 8:30 A.M. to 5:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). Alternatively, status inquiries should be directed to the receptionist whose telephone number is (703) 308-0196.

Kailash C. Srivastava, Ph.D.
Patent Examiner
Art Unit 1655
(571) 272-0923

September 5, 2006

RALPH GITOMER
PRIMARY EXAMINER
GROUP 1200